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STORAGE

TRANSACTIONS

OF THE

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

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TRANSACTIONS

OF THE

SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

APRIL, 1912.

VOLUME V. No. 6.

Proceedings of a Laboratory Meeting of the Society on Friday, March 15th, 1912, at 8.30 p.m., at the Laboratories of the Royal Army Medical College, Grosvenor Road, S.W.,

SIR WILLIAM LEISHMAN, F.R.S., *President*, in the Chair.

A large number of Fellows and visitors availed themselves of the kind invitation of the President and his colleagues at the commodious Laboratories of the Royal Army Medical College, and the meeting was a most successful one. A very representative series of specimens were shown by various Fellows of the Society and others, and abstracts of papers on some points of special interest were contributed to the meeting. Some of these, together with a description of many of the specimens shewn, are included in the present "Transactions." The meeting closed with a hearty vote of thanks to the President and his colleagues for the hospitality and excellent arrangements which had been made, the meeting being generally regarded as one of special interest.

AN ULCERATION NOTICED IN PERSIA IN THE DISCHARGE FROM WHICH SPIROCHÆTES ARE ABUNDANT.

By DONALD W. CARR, M.B.

The subject of this paper is a localised disease which I believe to be a pathological entity, and which up to the present, so far as I have been able to ascertain, has not been described.

Definition.—An ulceration becoming deep, fœtid and fungating, attacking various parts of the body, and characterised by the presence of immense numbers of spirochætes in the discharge.

History and general features of the disease.—In 1901 I saw a case of foul fungating growth of the hand which puzzled me. Its nature was not recognised at the time. I expected to find a fungus, and believed that I had found some in the discharge. The photo was taken, and a few smears kept for further examination. These were put by till 1908, when having found spirochætes in an unusual sore, they were re-examined in the light of further knowledge, and found to contain many of the same organisms. During the last three years I have collected in all eighteen cases presenting on the whole the same features, affecting the jaw, tongué, lips, cheek, neck, trunk, hand and foot in the following proportions :—

Lips,	5 cases.	Cheek,	1 case.
Foot,	4 ,,	Hand,	1 ,,
Jaw,	3 ,,	Neck,	1 ,,
Tongue,	2 ,,	Trunk,	1 ,,

In some cases the disease has been confined to the skin, spreading over a considerable area (cases 13 and 15), while in others it has eaten deeply into the tissues eroding the bone. In others again (cases 7 and 9) the whole hand and foot respectively were completely disorganised.

The chief features in all cases are very similar, a foul smelling fungating sore, generally eating deeply into the tissues, having overhanging edges concealing deep clefts. It emits a thin sanious discharge, containing a great number of spirochetes and rod-shaped

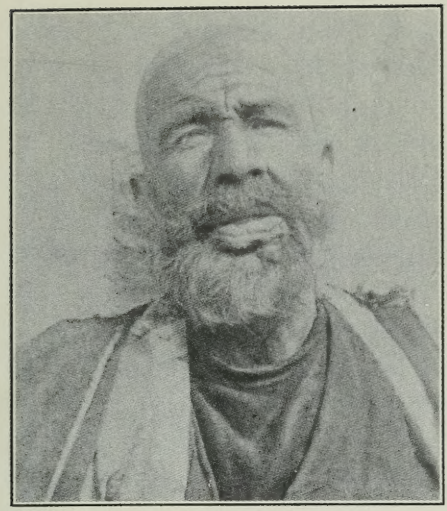

Fig. 1.

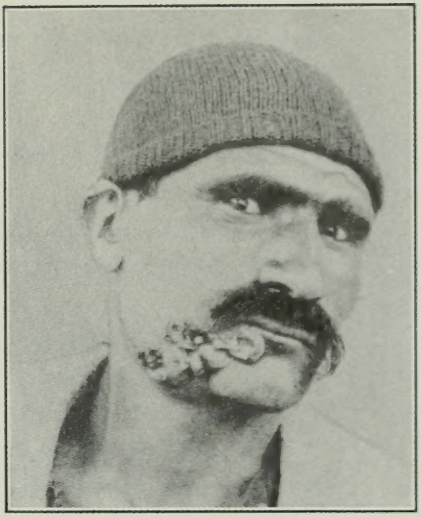

Fig. 2.

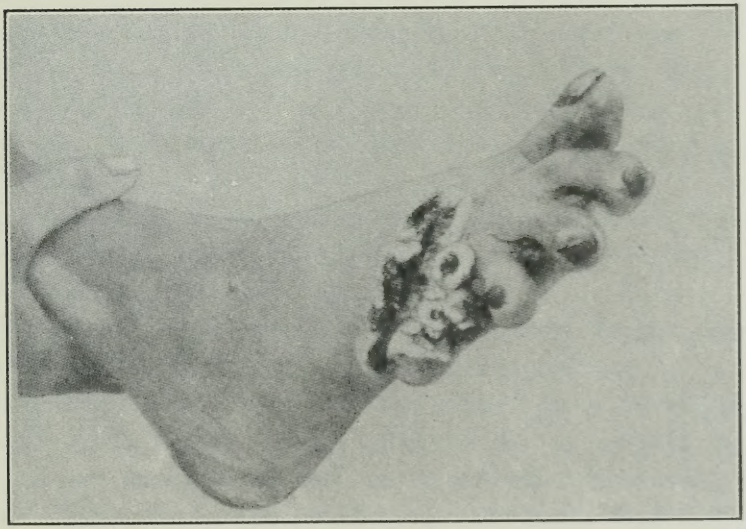

Fig. 3.

ILLUSTRATIONS TO ACCOMPANY DR. CARR'S PAPER.

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bodies containing chromatin particles. These latter bodies from their constant association with the spirochætes would seem to have some definite relationship with them.

The following is a short description of the cases :—

Case 1.—Hasan, 30, April 27th, 1908.

History.—Abscess under chin a year ago, opened by a Persian Doctor; pus evacuated but wound would not heal. Six months later a sinus opened in left check.

Present condition.—Left side of face much swollen. Two openings discharging very fœtid pus. An opening also on outer side of alveolus in mouth. Openings were enlarged. They led down to bone bare of periostium and eroded, but with no sign of necrosis or caries. Fever every night from 99 to 102, usually normal in morning. Examination of pus showed immense numbers of spirochætes.

Pot. Iod. was given internally. The wound showed no sign of improvement, and the patient went away.

Case 2.—Mohammed Ali, 20, October, 1910.

Six months ago had a carious tooth, lower right first bicuspid. Swelling on jaw appeared, which burst internally and later externally. On admission there was an opening discharging very fœtid pus. The sinus led to bare bone, which was rough and hard, not carious, and showing no signs of necrosis.

Under surgical treatment the sinus showed no sign of healing, and the patient went away.

The pus showed many spirochætes and also rod-shaped bodies. Some of the spirochætes were enclosed in leucocytes.

Case 3.—Hasan Aqa, 40, May, 1908.

Three years ago pain on left side of jaw. Abscess formed, burst outside, much pus discharged with two small fragments of bone.

Present condition: Jaws very stiff. Two small sinuses discharging very fœtid pus. Temperature normal. The sinuses led down to bare bone, hard and not perceptibly eroded, and no tendency to necrosis. A large number of spirochætes found in the pus. No improvement under treatment.

Case 4.—Taqi, 40, November, 1908; February, 1909; March, 1910.

About 1896 patient had a small abscess on lower lip, which burst, leaving a small ulcer, which would not heal entirely, though it did

partially, for there was scar tissue showing where it had healed. Two years ago two sinuses opened in the chin below free edge of lip. On admission there was an ulcer on free edge of lip on left side, and two sinuses below discharging stinking pus. The skin of chin was red, swollen, and painful. The openings led down to bare, hard, and somewhat eroded bone. The pus contained numerous spirochætes.

After vigorous scraping and the application of caustics the condition improved and was healing well, but patient would not stay any longer. Readmitted in February, 1909, and again in March, 1910, having again gone away before the sore was healed.

This time the condition was much worse. A large patch of soft tissues over the chin was gone, leaving the bone bare. The discharge, from which the spirochætes had almost disappeared when he last went away, was again swarming with them.

The previous scraping had removed a good deal of granular material not unlike hard herring roe.

General condition of patient was now much worse and the disease had extended up the side of the mouth and almost all over the chin. The smell was very bad and there was much pain. He went away and has not been seen again.

Case 5.—Karam Ali, 45, December, 1910.

Ulcer of lip. Twenty years ago a small pimple on lip. Persian doctor applied leeches. A small sore remained, but never got very bad. Three months after a Persian doctor gave a white powder to be applied. This caused ulceration.

On admission a hard ulcer on free edge of lip on right side.

Inside lip was a ragged ulcer with overhanging torn edges, not hard. Outside there was about $\frac{1}{4}$ inch of healthy skin below the hard ulcer, and below that a hard raised red patch with a small opening into it into which a probe could be passed from $\frac{1}{4}$ inch to $\frac{1}{2}$ inch. The pus from this is small in amount, has a bad smell, and contains many spirochætes. No enlarged glands could be felt.

The disease was freely removed as a V-shaped mass, the edges of the lip brought together. The patient went away apparently cured.

In addition to the spirochætes there were many short, thick, rod-shaped bodies. Many of these are united together to form spirochæte-like bodies.

One semilunar body was seen containing two chromatin bodies which appeared to have a flagellum.

Case 6.—Mother of T. M., February, 1911, ulcer of tongue.

Early in 1909 a small ulcer appeared on the right side of tongue, far back. Gradually got worse and edges became hard. Enlarged glands appeared at angle of jaw. Three doctors saw it and agreed in diagnosis of cancer, of which there seemed to be no doubt. Ulcer spread rapidly, and at end of six months was $\frac{3}{4}$-inch long and $\frac{1}{4}$-inch wide, and had eaten deeply into the substance of tongue. Operation was not advised, patient being the subject of serious heart disease. Mercury was given, and to our great surprise the sore began to improve. There has never been any suspicion either from the history or from the course of the disease that it could be syphilitic. At the end of eleven months from the commencement the sore was nearly well though the hardness never quite went away. The edges softened, the pain ceased and the glands subsided. In April, 1910, the tongue began again to become sore and ulcerated, and the edges became hard and the sore worse than it had ever been. Three molars which irritated the sore were removed, and the condition somewhat improved. At this time there was a deep hole in the side of the tongue extending inwards nearly $\frac{1}{2}$ inch, with a good deal of deep-seated hardness round it. The edges overhang the ulcer and have become soft and flabby. Discharge is very slight. The diagnosis remained quite open until certain points of resemblance having been observed between this case and cases 4 and 5, the discharge was examined and found to be swarming with spirochætes. The patient was put on a course of mercury and arsenic, and the sore again improved very much. The acuteness passed off though a deep hole remained in the tongue, with soft flabby overhanging edges.

Long filamentous bodies were rather a marked feature in this case (? some form of leptothrix), and there were also many rod-shaped bodies which have been so constantly associated with the spirochætes.

Subsequent history: An enlarged gland formed at the angle of the jaw and remained quite hard. There was much pain from this, and the patient became worn out from the constant pain. After about two months this softened and was opened, a large quantity of pus being evacuated. No spirochætes were found in this but a pure culture of

streptococcus. The patient shortly after this died, the tongue remaining in the same condition.

Case 7.—Ahmad, 50, November, 1901.

In 1896 patient noticed a small lump on back of right hand, the size of a pea. This spread over back of hand, and in 1899 was thoroughly scraped. Material resembling the hard roe of a herring was scraped away. The hand improved and seemed as if it was going to heal when patient insisted on going away. He returned in 1901 with hand much worse than before. It was wholly disorganised and almost shapeless. There were a number of sinuses discharging fœtid pus. Amputation was performed.

Smears were taken and put aside, and subsequent examination several years later showed many spirochætes and rod-shaped bodies.

Case 8.—Husein, 20, December, 1908, ulcer of foot.

History: One month ago the left foot swelled. Under treatment by a Persian doctor the swelling softened and burst, discharging pus. On admission there were two small undermined ulcers on the dorsum of left foot, the discharge from which showed many spirochætes. They were freely scraped and treated with strong antiseptics. They healed in about a month.

Case 9.—Mirza Mohammad Ali Khan, 60, disease of foot.

Seen in 1908 with a Persian doctor. Foot was much swollen and was discharging stinking pus out of several sinuses. He had been under treatment for several months. Foot much disorganised. Exploratory operation was advised with a view to amputation if it should be found to be necessary. This was declined, and patient became rapidly weaker and died a couple of months later. Many spirochætes and rod-shaped bodies were found in the pus.

Case 10.—Haji Mehdy, 40, March, 1911, ulceration of lip. *(Fig. 1.)*

Began as a small pimple on the left side of lip which he used to bite with his teeth. It gradually spread.

Present condition: Extensive ulceration involving three-quarters of lip and eating deeply into its substance. Two or three deep cracks run deeply into lip. There is much hardness. On the left side of chin is a soft swelling from which pus can be squeezed through an opening just above. Discharge teeming with spirochætes.

Refused surgical treatment. Donovan's solution was given daily

and the deep cracks powdered with calomel. No improvement resulted.

Case 11.—Karam Ali (Sehdeh), 25, affection of neck.

Three years ago toothache in third left molar of lower jaw. A swelling appeared outside, which burst and discharged.

Present condition: A patch of unhealthy undermined skin about angle of jaw, 2½ inches by 2½ inches in extent, with two or three small openings discharging thin, unhealthy looking pus. The appearance was very suggestive of actinomyces. There was no opening inside the mouth. The pus was found to contain large numbers of spirochætes and rod-shaped bodies which have been so constantly found in conjunction with spirochætes.

On glucose agar nothing grew except cocci and a few bacilli. Patient so far has refused to come for any treatment.

Case 12.—Naqd Ali, 30, March 17, 1911, ulcer of lip.

A year ago a small pimple appeared on right side of lip. Leeches were applied by Persian doctor. The sore gradually spread. An ointment was then applied which made it much worse.

On admission there was extensive ulceration along free edge of lip for three quarters of its extent and eating deeply into the lip. Edges hard and everted. Thin unhealthy looking pus coming from it, but not in any great quantity. A probe could be passed nearly half an inch into the sulcus formed by the deep ulceration on the free edge of lip. No history of syphilis nor did the sore resemble that disease. The pus was swarming with spirochætes and rod-shaped bodies containing chromatin particles. The lip was removed as far as it was involved by the disease, being restored from the cheek.

Case 13.—Jahan Sultan (female), 30, March, 1911.

Two years ago had sores on leg, abdomen, and breast. These got well after scraping. Four months ago sores came on left abdominal wall and outer side of right breast. Sore on abdomen is now 4 inches by 3 inches, slightly raised above service. Thick granulation tissue deeply worm eaten in appearance and emitting an unpleasant odour. Slight purulent discharge.

The sores were scraped and smears from the scrapings showed many spirochætes. The deep tissues had not become affected and the sores healed.

Case 14.—Amir Qadir, 40, March, 1911, ulcer of tongue.

For three years off and on there has been a small sore on left side of tongue about level of first molar. Steadily worse last three months. Now a large sore on left side of tongue 1 inch by 1½ inch, covered with scraps of whitish membrane. Deep in centre, base hard. There is a healing edge with thin red line of new epithelium along upper edge, but sore looks on the whole unhealthy. The pus contains many spirochætes and rod-shaped bodies so frequently found in association with the spirochætes.

Mercury and arsenic have been tried without much benefit.

Case 15.—Fatimeh (female), 45, April, 1911, ulcer of foot. *(Fig. 3.)*

Foot burnt when a child, contraction followed. Admitted in November, 1910, with ulcer on outer side of foot. This healed under treatment.

In March, 1911, patient returned with ulcer broken down and growth over roots of two outer toes resembling epithelioma (see photo). Growth easily removed by scraping, the outer toe being also removed, the bone being almost eaten through. Discharged May 6th quite cured. Medicinal treatment was black wash locally and Donovan's solution internally.

Case 16.—Husein, 30, March, 1911, ulcer of sole of foot.

Foot burnt when a child, never quite healed. Always small ulcer left. Lately has gradually increased.

On admission extensive ulceration on sole of left foot from middle of sole to heel and well to outer side of heel. A fungating stinking granular growth thought to be probably epitheliomatous.

Discharge found to be swarming with spirochætes and rod-shaped bodies, the latter being specially numerous.

On April 27th ulcer was freely removed, the base being treated with sulphur gauze. It is now slowly healing and no more spirochætes can be found in the discharge.

Case 17.—Husein, 30, ulcer of lip and jaw. *(Fig. 2.)*

About October last patient got an ulcer on outer part of right side of lower lip near angle of mouth. Spread rapidly. No cause known. Present condition: Much thickening over right side of lower jaw about level of facial artery. Fungating ulcers emitting a foul smell extend from here to corner of mouth. Thin unhealthy discharge swarming with spirochætes and rod-shaped bodies.

The sore was freely scraped and treated with sulphur gauze and became healthy looking and was healing well but patient would not stay any longer.

Case 18.—Riza Kuli, 50, June, 1911, ulcer of cheek.

Small pimple on right side of nose fifteen years ago. Remained quiescent for some years but never went away. On admission a deep ulcer on right side of nose 1 inch by ½ inch extending well into angle of eye. Taken at first for rodent ulcer, but edges though hard were in parts undermined, the skin overlapping the sore. A little thin discharge containing many spirochætes and rod-shaped bodies.

The edges and sides were freely cut and scraped away and the ulcer packed with sulphur gauze. It appeared healthy and was healing when patient insisted on going away.

ETIOLOGY.

Age.—None have been seen so far in children, the ages varying from about 20 to 60.

Sex.—More have been seen in men (15 to 3). This may be because they have been more looked for in men.

Nationality.—All have been in Persians. No cases have been observed so far in Jews, Armenians, or Parsees, all of which nationalities are found here.

The cases, however, have been too few to say anything definite on these points.

Nothing can be said at present as to the mode of infection. The fact that the affection has occurred on such positions as the tongue and the sole of the foot make it unlikely that it is due to the bite of an insect. In two of the cases the patient had had a small sore for a long time which gave no trouble, and increased little if at all in size until cut by a Persian Doctor—presumably with a dirty knife—after which the sore became rapidly worse, and developed its characteristic appearance.

PATHOLOGY AND MICROSCOPIC APPEARANCES.

The constant feature of all the cases is the presence of large numbers of spirochætes. The sores are usually deeply fissured and the skin undermined. The edge of a fissure being raised by a probe, a cleft may be seen extending from one-sixteenth inch to a quarter inch into the tissues or even more, the deeper parts being slightly hollowed out and

containing a small quantity of thin, foul smelling discharge which swarms with spirochætes.

The spirochætes vary much in size. My drawings have all been made with Ashe's camera lucida with a Leitz one-twelfth oil immersion object glass and No. 12 compensated eye piece, giving about 1,400 diameters. Many are extremely fine, while others are coarse and have a double outline, and contain one or more chromatin bodies. Others contain a central clear spot. Some can be seen to be apparently dividing transversely.

Associated with the spirochætes are large numbers of rod-shaped bodies, some thick with blunt ends, slightly curved, and usually containing two chromatin particles. Others have pointed ends and take the blue rather than the red of Geimsa's stain, and contain two rather darker blue particles in them.

The constant association of these bodies with the spirochætes, whereas they are not seen in sores which contain no spirochætes, strongly suggests that there is a close relationship between the two.

Some of the discharge from the lip of Husein (Case 17), grown in citrate of soda solution, showed after eleven days a few spirochæte-like bodies much larger and thicker than the other spirochætes, and probably a further development of these.

Sections have been cut from pieces of tissue from three cases, and in one of them, Naqd Ali (Case 12), spirochætes have been demonstrated in the tissues.

No spirochætes have been found in the blood.

The relative count of leucocytes has not been taken in every case, but where it has been taken it showed no marked deviation from the normal.

A large number of other sores of all sorts have been examined, but no spirochætes have been found except in the cases mentioned in this paper, which also present other striking features.

DIAGNOSIS.

1. From other diseases associated with spirochætes.

From Syphilis.—The appearance and history of these sores is not as a rule suggestive of syphilis in any of its stages.

The spirochæte differs widely from *S. pallida.* It stains easily, *e.g.* with methylene blue, it is coarser and has fewer and larger turns, while

the immense numbers in which the organisms are present in some cases would exclude *S. pallida*.

From Yaws.—The history and appearance of these sores is entirely different from that of yaws, a disease which, as far as I am aware, is not found in Central Persia.

From Granuloma of the Pudenda.—The position of the sores, none of which have been on the pudenda, exclude this.

2. *From Oriental Sore.*—A few of the cases might possibly at first sight be mistaken for oriental sore, which is very common in Persia, but the microscope at once decides the matter, no Leishman-Donovan bodies ever being found in the sores while they swarm with spirochætes.

3. *From Cancer.*—Some of the cases have been very suggestive of cancer, especially case 6, ulcer of the tongue. The history and later appearance of these, however, has differed markedly from cancer.

4. *From Actinomyces and Mycetoma.*—Some cases, such as case 9 of the foot and case 11 of the neck, suggested Madura foot and actinomyces respectively. The microscope set the matter at rest.

PROGNOSIS.

The prognosis on the whole is serious. Some have gone from bad to worse, in spite of all treatment. Of the 18 cases, 6 are believed to be cured, 3 by scraping and 3 by free removal.

TREATMENT.

Iodide of potash has had no effect. Mercury and arsenic in one case (No. 6) seemed to have a beneficial effect, and not only kept the disease in check but the condition improved very materially, though complete cure did not result.

No other treatment which has been tried has seemed to be of any use except very thorough scraping and treatment with caustics, or free removal where this is possible.

I have not yet had an opportunity of trying the effect of salvarsan, but I have obtained a small quantity and hope to try it on the next case that I see.

GENERAL CONCLUSIONS.

It is well known that spirochætes are found in immense numbers in the mouth in certain positions such as in the soft creamy deposit round

the neck of dirty teeth and they are very easy to demonstrate in this deposit. The earlier cases I noticed were in connection with the mouth, and I thought that the spirochætes found in the discharge might be merely saprophytic, and that the *S. Buccalis* and other spirochætes from the mouth having found a favourable soil in the diseased tissues had grown luxuriantly. The finding, however, of similar organisms in sores far removed from the mouth seems to render this explanation unlikely.

The fact that we have here a series of sores affecting various parts of the body which have in themselves attracted attention by their unusual appearance, history and course, and led to search being made for a definite cause, together with the fact that spirochætes have been found in abundance in the discharge from all of them—organisms not usually found in sores and ulcers—leads me to believe that we have here a definite pathological entity, due to the spirochætes, which, as far as I can ascertain has not been hitherto described. It is highly probable that the disease is not confined to this district round Isfahan, but that if it is looked for it will be found to occur over a much larger area of Central Asia.

N.B.—Since writing the above paper I have seen the paper on *Ulcus tropicum* by KEYSSELITZ and MAYER, and it is possible that the disease I have noticed is identical with what they have described. The cases I have noticed, however, do not seem quite to agree with the description they give.

The PRESIDENT, in commenting on Dr. CARR'S paper stated that he regarded it as a case of *Ulcus tropicum*, a specimen of which he was showing, derived from a blood film taken from a native of Sierra Leone. (See No. 13, page 229.)

A RAPID METHOD OF DIAGNOSIS IN MALARIA.

By J. CROPPER, M.D.

The following is a method which I have found useful in practice, and this must be my excuse for bringing it before the Society of Tropical Medicine and Hygiene.

It has often been said to me that it is impossible to examine every case of malaria in out-patient practice, owing to the length of time required; but I feel that in order to become thoroughly acquainted with the diseases of any locality this is necessary.

I have not seen the method described, it is as follows :—

Thick films are made on the slide without even a coverslip, so thick that the blood when allowed to run to one side is seen of a bright red colour. This is rapidly dried and examined directly under a drop of cedar oil and a $\frac{1}{12}$ in. immersion. (The drying of this film causes the only delay).

In a dry country such as Persia, films will dry in the open air without any special treatment in about half a minute. In a damper climate they should be exposed to the sun, turned upside down. In damp and cold weather they should be dried gently over a spirit flame. In any case one can begin the examination before the *whole* film is dry, and very often the information got is sufficient before the thicker edge is properly "set."

I have often proved the existence of malaria (verified of course by a properly stained slide), in one minute by the watch from the time of drawing blood. The thicker part of the film is best examined first, and from the character of the pigment the species of malarial parasite can after a very little practice be diagnosed in most cases with great ease, almost as easily as in a wet film.

If no characteristic pigment is found in two minutes, the case is most likely not one of malaria; in any case of doubt of course the other methods are available, but probably not more than one case in ten of untreated malaria would escape detection.

I do not pretend for a moment that this is a method by which beginners can study malaria any more than that of Sir RONALD ROSS;

but it is very rapid and accurate, and one moreover which avoids nearly all the pitfalls inseparable from those more commonly used, and indeed from Sir RONALD ROSS's method, which I have tried. At starting of course a student should carefully compare his dry slides with slides carefully stained in the usual way. This gives confidence and is a valuable check to the work.

I have no hesitation in saying that once this method is given a fair trial, it will be found of real use in out-patient work in tropical countries, where stress of work makes every minute of the greatest value.

NOTE.—The diffuse and fine dots of tertian, the compact and coarser dots of quartan, and the peculiar arrangement of the pigment in the crescents in tropical malaria are very characteristic, not to mention pigmented leucocytes. They are as well seen as in a wet film, the chief point being to be sure that the pigment is on the same level as the red corpuscles, and disappears totally on focussing up or down.

SCHISTOSOMUM JAPONICUM INFECTION IN A EUROPEAN.

By Fleet-Surgeon BASSETT-SMITH.

Specimen A ... Blood film noting per cent. Eosinophiles.
„ B ...
„ ... Film showing ova in stool.

The case was that of a young European aged 24, who was serving in a man-of-war up the Yangtse.

History.—While at Hankow on the 18th June, 1911, he with four others went for a picnic to Seven-mile Creek, and they all bathed in a flooded area; the water was clear but not deep.

All subsequently were attacked with fever and so-called "bloodworm disease," two others so severely that they returned to England, two mildly, remaining at Hankow.

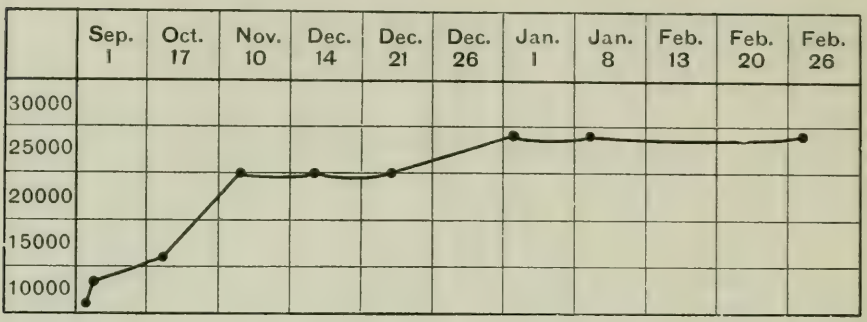
Following the fever he suffered from constipation and neuralgia, became anæmic and thin. In September a marked eosinophilia was present and liver was slightly enlarged. At Yokohama Hospital large ova containing embryos were found in the stools and the blood content was very abnormal; a decrease in red cells with a great increase of eosinophiles.

On arrival in England in December, six months after the onset of the symptoms, he was sallow in appearance, somewhat emaciated, the liver slightly enlarged, but the other organs normal. The bowels were constipated, but the stool contained occasional fragments of mucous.

Ova with living embryos were found (·055 mm. × ·035 mm.) in small numbers. Beyond some debility and slight œdema of the ankles there were no symptoms. He was treated with beta-naphthol.

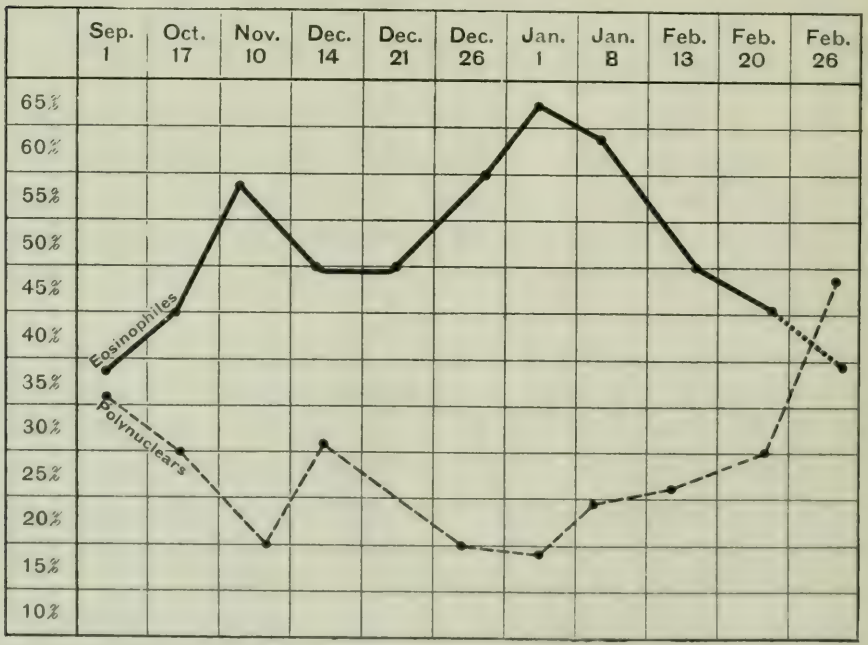
As will be seen by the chart the total white count still keeps at a very high level, but the eosinophiles having reached 68 per cent.

have now dropped to 38 per cent., the polynuclear cells increasing proportionately.



The presence of the disease in a European is very rare—a case was described by MANSON in the *Journal of Tropical Medicine* for November 16th, 1908.

The extraordinary high relative eosinophile count is, I believe, unique, which with the frequent blood observations taken renders the case of greater interest. The patient is still under observation.



SOME HUMAN ENTAMŒBÆ.

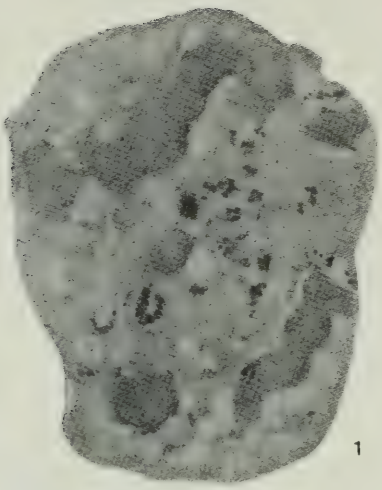
By W. CARNEGIE BROWN, M.D.

Under these microscopes you will see several specimens of intestinal amœbæ. They are (1) *Entamœba histolytica*, which was taken in this country from a case of amœbic dysentery, recently contracted in South China. A small film of rectal mucus and blood was spread on a slide, fixed by methylic alcohol and stained by GIEMSA'S slow process. Similar films fixed wet, that is to say, by SCHAUDINN'S corrosive sublimate and alcohol solution and stained by HEIDENHAIN'S iron hæmatoxylin, give a less definite picture of the organism; and, generally speaking, in my hands wet fixation of amœbæ has been less successful than the rapid alcohol and also than the osmic acid vapour methods. In this specimen you may see very clearly the differential staining of ectoplasm and endoplasm, the structureless character of the former and the granular formation of the latter. No nucleus is visible because almost the whole of the endoplasm is stuffed with red blood corpuscles in various stages of digestion. Some of them are just being caught up, and although the process of fixing has caused considerable retraction, and has made the organism assume a more circular outline than it ever takes in active life, it is still possible to follow quite distinctly the method by which the erythrocytes are englobed by the hyaline pseudopodia, and the summary manner in which they are thrust into the very interior of the parasite. There are some 25 red corpuscles or their remains in this entamœba, each of them being about 7μ in diameter, the organism itself measuring about 35μ. The specimen shows an exceptionally large parasite, but one that is by no means unusually repleted, for the consumption of blood by *Entamœba histolytica* is not only extraordinarily copious, but very rapid. When so great a number of corpuscles are swallowed with such apparent ease, one might expect to find amongst them a leucocyte or two, but the absorption of leucocytes by entamœbæ has never been noted by me, nor, so far as I know, by any other observer. The explanation of this biological fact is not very clear; but it is possible that *Entamœba*

histolytica, in spite of notorious voracity, draws the line at swallowing what may be after all a not very distant relative.

I should like to say that the difficulty of demonstrating intestinal entamœbæ, either in the living or fixed and stained condition, is much exaggerated. After a little practice it is impossible to miss them, and if thick slides, which have been dipped in hot water are used for fresh specimens, the movements of the organism can be readily followed in ordinary room temperatures for two or three hours. Except in very cold weather, a warm stage is unnecessary. As to stains, a modification of ROMANOWSKI is essential, since, for differentiation of species, nuclear staining is very important, and I find that one routine method for practically all specimens, viz., GIEMSA'S original process, is the best. As you see, with its use one should not mistake either the nature of the organism or its contents. The red blood corpuscles, which in this specimen are lying free in the blood-stained mucus in such quantities, take on an orange-red shade, which they retain after they are englobed, although it gradually becomes paler and dingier as digestion goes on. One occasionally sees some débris and granular matter extruded by the living organism, but apparently the whole corpuscle, hæmoglobin and all, is assimilated by *Entamœba histolytica* without difficulty and without refuse.

Under the next microscope you will see a fairly representative specimen of (2) *Entamœba coli*—an organism which is a frequent, and probably a harmless denizen of the alimentary tract. Views still differ widely as to the true place in biology of this parasite, but personally I am of opinion that there are very strong grounds for its specific and pathogenic differentiation from *E. histolytica*. As you know, the principal morphological points of distinction are that in *E. coli* the protoplasm is not clearly separated into ectoplasm and endoplasm, that the pseudopodia are granular and softer looking, and that the nucleus is bolder and contains more chromatin. Vacuoles—non-pulsating, of course (pulsating vacuoles being distinctive of free-living amœbæ)—can generally be seen, but rarely, if ever, does *E. coli* englobe blood corpuscles. Certainly it does not penetrate the intestinal membranes or tunnel through the submucosa like *E. histolytica*, and to my mind, it is on the examination of fresh sections of intestine or fragments of slough that a final verdict as to the species of an entamœba must rest. Nothing



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2

3A

3B

ILLUSTRATIONS TO ACCOMPANY Dr. CARNEGIE BROWN'S PAPER.

else is decisive; in the fresh condition, the two organisms may resemble each other very closely, and stained specimens are often even more difficult to differentiate when there is no ingestion of blood corpuscles. Reproduction differs widely, but it is so difficult to follow, that as a practical method for clinical distinction it is useless. On the other hand, if a fresh fragment of sloughed intestinal tissue, such as may often be found in dysenteric blood and mucus, is teased on a slide with a little warm saline solution, or if it is shaved into thin sections with a warm and moist razor, the organisms are readily seen, and all the characteristic distinctions which were originally demonstrated by SCHAUDINN can be accurately followed.

Under a third microscope you will see a specimen of still another entamœba, which in certain countries appears to be frequently associated with amœbic dysentery, but which most of us have hitherto regarded as being of doubtful pathogenicity, and which few of us have, in fact, identified. It is (3) *Entamœba tetragena*, and the specimen was sent to me by Dr. JAMES of the Panama Canal Commission. The patient was a Spaniard who had well marked dysenteric symptoms from which he had suffered at intervals for some years, and enormous numbers of the organism and its characteristic four-lobed cysts are to be seen in these smears of rectal mucus. The chief distinctive points which are claimed for *E. tetragena* are (*a*) Size; that is to say it is much smaller than *E. histolytica* or *E. coli*—about 12 to 15μ diameter as compared with 20 to 30μ. (*b*) The nucleus in young specimens is well defined and contains considerably more pigment than is seen in either *E. histolytica* or *E. coli*. (*c*) Afterwards, the nuclear envelope is frequently ruptured or missing, and the chromidia, as in the specimen now on view, are scattered in clumps through the protoplasm. (*d*) The cysts have four nucleolar masses or lobes.

Now, with regard to these features, the first—size—has little specific value. In many cases of *E. histolytica* infection, all the organisms are small; in many others they are all or nearly all of a normal diameter, yet in others they are irregular; and, as a general rule, it is unsafe to place much reliance on size (which depends on nutriment) as a distinguishing feature of any species of intestinal protozoan. Chromatin, too, both in nucleus and cell-substance is very variable in quantity, and although the fragments of coarse chromatin agglomerated round

the nucleus are very characteristic, it would be going too far to say the peculiarity is clearly specific. Again, in the original descriptions of the organism by HARTMANN and BENSEN, great importance was attached to the large chromidial masses which seem to float out of the nucleus and to diffuse themselves in the cell protoplasm, probably as a preliminary to schizogony or encystment; and in the specimen before you this can be very clearly seen. Personally, I confess I have always been very doubtful as to the nature of this process, and was inclined to agree with those protozoologists who hold that the phenomenon is simply a result of the nuclear envelope being ruptured during fixation; but the appearance is so constant, and, in fact, so characteristic of special cases, that (with other features) it would appear to be almost certain that we have to deal with a distinct species. In short, a careful study of these very beautiful preparations of Dr. JAMES'S leaves little room for doubt that, although the crucial test of observation of fresh specimens in fresh tissue is still unfilled, this is either a new species or that *E. tetragena* has established what is at least a provisional claim to pathogenicity.

However, if it is admitted that *E. histolytica* and *E. tetragena* stand definitely in the relationship of cause and effect to amœbic dysentery, the list of nocuous entamœbæ is, so far as we know, exhausted with them. The evidence on which pathogenicity has been claimed for other varieties is mostly very slender, and even if the authors' own descriptions form the sole basis of judgment, it is very difficult to find any marked differences between the organisms which they depict and undersized specimens of *E. histolytica*. Probably in certain countries, or at least in certain districts, there are strains of entamœbæ which cannot be specifically detached from the more familiar varieties, but which nevertheless possess some characteristics that link them together as almost distinctive groups. Among these organisms I should be inclined to include the variety described by NOC as occurring in Saigon, and perhaps the commonest of the entamœbæ found in India by GREIG, although the vegetative stages—as opposed to the cystic—of both these parasites have also undeniable resemblances to *E. tetragena*. With regard to these cystic forms—plenty of which are to be found in the smear before you—the typical four-nucleated cyst described by VIERECK and HARTMANN is much less frequent than a cyst that has apparently

only two lobes, for nuclei they can scarcely be called; but it must be remembered that cysts are globular or very nearly so, and that it is not always easy to focus through deeply stained specimens. The cyst of *E. coli* is generally quite clear and hyaline with a thick outer membrane, and that of *E. histolytica*, though granular and often darkly shaded, has not like that of *E. tetragena* a septate appearance.

ILLUSTRATIONS, by A. J. E. TERZI, facing page 221.

Fig. 1.—*Entamœba histolytica* in rectal mucus, stained by GIEMSA. Longest diameter 35μ. The endoplasm which stains lightly contains a number of fresh erythrocytes, and much granular matter, the remains of previously englobed corpuscles. In this specimen the nucleus is clearly visible.

Fig. 2.—*Entamœba coli* in rectal mucus. Diameter 19μ. Ectoplasm and endoplasm not differentiated, and nucleus deeply stained. Note the finer grain and the vacuolation of the protoplasm. The specimen is smaller and more spherical than usual.

Fig. 3A.—*Entamœba tetragena* (cystic form). Diameter 6μ. Stained by HASTINGS' method.

Fig. 3B.—*Entamœba tetragena* (vegetative form). Stained by HASTINGS' method. Diameter 13μ. The ectoplasm and endoplasm are clearly differentiated; the nuclear contents have escaped, and several bundles of chromidia may be seen in the cell protoplasm. The empty nuclear envelope is placed a little excentrically.

THE DEVELOPMENT OF *FILARIA IMMITIS* IN THE MOSQUITO.

By G. C. LOW, M.D.

Dr. G. C. Low showed a series of sections illustrating the development of *Filaria immitis*, a parasite of the dog, in the mosquito. These sections were made in the Roman Campagna in the summer of 1900, and confirmed the work done by GRASSI on the same subject just before.

The *F. immitis* is a filarial parasite of the dog, the adults of which inhabit the right ventricle of the heart, the embryos the internal and peripheral blood streams. A severe infection of adults in the heart may eventually kill the dog. The embryos may be found in the peripheral blood by day as well as by night, and they resemble somewhat closely both as regards morphology, length and breadth, the embryo of *F. bancrofti*, the commonest of the human filarial parasites. The point of distinction, however, is that they do not possess a sheath like the latter. The length of these embryo filariæ of the dog may roughly be taken as about one-ninetieth of an inch, while their breadth is somewhere about that of a red blood corpuscle. GRASSI first showed that the intermediate host for the dog filaria in Italy was the *Anopheles maculipennis*, the embryo developing not in the thoracic muscles as in the human filaria (*F. bancrofti*), but in the malpighian tubes. The specimens shewn were a series of sections made by Dr. Low to confirm GRASSI'S work. Later BANCROFT in Australia demonstrated that the *F. immitis* embryos of those parts could also develop in the malpighian tubes of *Culex fatigans*, the common brown house mosquito of Australia, and it is quite possible that other species of mosquitoes may function in other parts of the world, though so far there is no record of such having been tried. The technique of the experiments was simple. *A. maculipennis* mosquitoes bred from larvæ were applied in test tubes to the abdomen of a brown pointer dog which had numerous filarial embryos circulating in its peripheral blood. The mosquitoes fed readily from the test tubes even in bright sunlight, and then they were transferred to proper mosquito houses, the date of biting being carefully kept. From day to day, or every second day or so, specimens were removed, killed by dropping into alcohol, hardened, and then embedded in celloidin. Finally sections were cut.

Fig. 1.

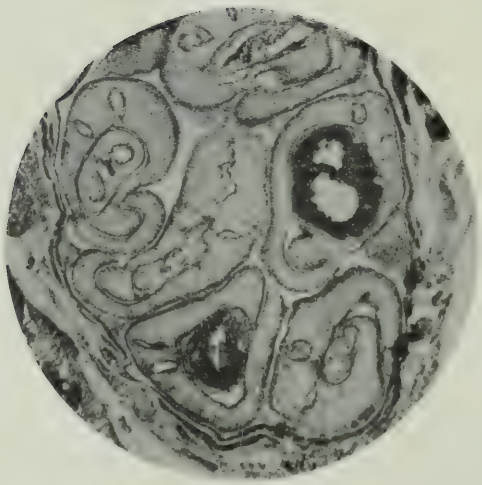

Fig. 2.

ILLUSTRATIONS OF SPECIMENS SHEWN BY Dr. T. S. KERR.

MAJOR MARSHALL'S DEMONSTRATION.

Dr. G. C. Low showed specimens of amœbæ that Major MARSHALL had sent from Edinburgh. These were taken from a case of amœbic dysentery found in Scotland, in a patient who had never been out of Scotland. The case had been published in the *Edinburgh Medical Journal* for March, 1912, and it was the second case reported in Great Britain.

DEMONSTRATION BY T. S. KERR, M.B.

The following among other specimens were shewn :—

(*a*) A blood film from a native of British Guiana, with a double infection of microfilariæ, *demarquii* and *perstans*, both present in very large numbers. In the whole film, of about 1 c.mm. of blood, there were 709 microfilariæ, and in the field shown ($\frac{1}{2}$ in.) eighteen could be seen.

(*b*) *Trypanosoma gambiense* from the cerebro-spinal fluid of a monkey, the trypanosomes being present in vast numbers.

(*c*) A case of blood crisis, occurring in Lardaceou's disease, in a patient who had served five years in India. The remarkable feature in the films was the extraordinary number of nucleated red cells, chiefly normoblasts, though a few megaloblasts and poikiloblasts were also present.

(*d*) A male and female *Schistosomum japonicum* in coitu. *(Fig. 1.)*

(*e*) A transverse section of a mesenteric vessel shewing several specimens of *S. japonicum* blocking up the lumen of the vessel. Several females can be seen encircled by males ; the mode of locking of the incurved sides of the males so as to form the gynecophoric canal being clearly shown. Ova can be seen in the uterus of several of the females. Probably, six specimens are represented in the section, but it is difficult to tell the exact number, as some may be doubled on themselves and would thus be represented by two sections. *(Fig. 2.)*

DEMONSTRATION BY THE PRESIDENT—

SIR WILLIAM LEISHMAN.

1. The cultural forms of the parasite of *Infantile Kala-Azar—Leishmania infantum.* Stained films were shown under the microscope, illustrating various forms of the flagellated organisms which develop in cultures on Novy-McNeal medium, a low power view of one of these films displayed well the characteristic rosette formation, frequently noticed, in which the flagella are invariably directed towards the centre of the rosette. The films were made from a culture of the 12th passage from that originally received from M. NICOLLE, at Tunis.

2. *Tick Fever.*—In illustration of this were shewn the following specimens:—

(*a*) Living specimens of *Spirochæta duttoni* from the blood of an infected mouse, by dark-ground illumination.

(*b*) Dissection of the tick—*Ornithodorus moubata*—to display the principal organs, such as the alimentary sac and its diverticula, the malpighian tubules, the salivary glands, the ovary, etc.

(*c*) Specimen shewing the granule clumps, derived from the spirochætes, lying in a minute ovum projecting from the edge of the ovary.

(*d*) Specimen shewing the young spirochætes in association with the granules from which they have apparently developed. From a young nymph which had been kept for 5 days at a temperature of 37C. some weeks before dissection.

(*e*) Specimen shewing young spirochætes and granules in the malpighian tube of a young tick, similary treated as in "*d.*"

(*f*) In contrast to the above specimens two others were shewn demonstrating: (1st) The intra-corpuscular bodies described by BALFOUR in the *Spirochætosis of Sudan Fowls;* and (2nd), the granule clumps which he has found in the malpighian tubes and other tissues of the tick whose bite transmits this disease—*Argas persicus.* (Inoculation of these granules, in BALFOUR'S hands, has given rise to spirochætosis in the fowl, as Sir WILLIAM LEISHMAN had

shewn to occur in the case of the *duttoni* granules of ornithodorus when inoculated into the mouse.)

3. Blood film from a dog shewing heavy infection with *Babesia* (Piroplasma) *canis*. (Prof. NUTTALL.)

4. Blood film from a horse shewing infection with *Nuttallia* (Piroplasma) *equi*. (Prof. NUTTALL.)

5. Blood film from a jerboa shewing specimens of *Hæmogregarina balfouri*. Sudan. (Dr. A. BALFOUR.)

6. Blood film from an Indian squirrel shewing the parasite found by Captain PATTON—*Hæmogregarina funambuli*. (Capt. PATTON.)

7. Blood film from a fowl in Annam, shewing a specimen of *Leucocytozoon sabrazesi*, described by MM. MATHIS and LEGER.

8. *Histoplasmosis*.—Two specimens were shewn of the organism described by Dr. DARLING in cases of this disease in Panama, the first was a smear preparation from the spleen shewing numerous examples of *Histoplasma capsulatum*, both free and enclosed in large mononucleated cells, the other, a section of the liver from the liver of the same case, shewed intense disorganisation of the organ and numbers of the parasites lying in large cells, probably of endothelial nature.

9. *Filaria volvulus*.—Two specimens were shewn, the first sent by Dr. HANS ZIEMANN from the Cameroons, displayed the microfilariæ in a smear preparation made from a gland; the other, a specimen from the Congo sent by Dr. E. BRUMPT, displayed in a section the adult parasite lying in the tissues and the immature microfilariæ in great numbers seen in the transverse sections through the uterus of the female.

10. *Filaria loa*.—Section through the aponeurosis of the thigh of a native in the Congo (Dr. BRUMPT), shewing the adult parasite containing immature microfilariæ *(Microfilaria diurna.)*

11. *Blood film from an Annamese fowl*, shewing the microfilaria described by MM. MATHIS and LEGER, lying in an exceptionally large and loose sheath.

12. *Trypanosoma granulosum*.—Specimen from the digestive tube of a leech—*Hemiclepsis*—shewing the developmental forms. (Dr. E. BRUMPT.)

13. *Ulcus tropicum*.—Blood film taken from the neighbourhood of a phagœdenic ulcer in a native at Sierra Leone (material sent by the late Capt. HALLAM HARDY, R.A.M.C.). Numerous spirochætes and fusiform

bacilli are present. In this and other films from the same case it was possible to trace all intermediate stages between the *Bacillus fusiformis* and the spirochæte (? *vincenti*), the bacilli lengthening out into leptothrix filaments, which eventually become curved and thrown into undulations, and assume the same staining characters as the rest of the spirochætes.

14. Smear preparation from the spleen of a calf, Uganda, showing *Koch's bodies* (Plasmakugeln, "blue bodies"), supposed to have some causative connection with the disease known as East Coast Fever. (Specimen by Colonel Sir DAVID BRUCE.)

DEMONSTRATION BY CAPT. J. C. KENNEDY, M.D., R.A.M.C.

The Society will remember that Dr. THOMAS, at a meeting held in November, 1909, showed specimens and demonstrated a case of œsophagostomiasis occurring in a native of the Amazon State. This is only the second time the condition has been found in man, but it is a common affection in monkeys. I therefore thought it would interest the Society to see actual specimens of the infection as it occurs in monkeys.

The monkeys are the common *Macacus rhesus*, and were some of a large consignment that the Malta Fever Commission had sent from Calcutta to Malta. The majority of these monkeys were infected, and it is possible that this is accounted for by their close confinement in crates during shipment.

The symptoms during life are: diarrhœa, at first slight but later very severe, progressive emaciation and pain, which is evidenced by the manner in which the animal sits huddled up, pressing his arms into his abdomen. When death occurs it is due to a peritonitis, local or general, caused by the rupturing of one of the larval cysts into the peritoneal cavity.

Post-mortem, the large intestine from the cæcum downwards is found riddled with cysts, each of which contains a larval worm (sometimes two). These cysts, for the most part, are submucous, but a large number present on the peritoneal surface of the intestine; when in this situation they are always attached to the longitudinal muscular bands, and may be arranged like a festoon. I look upon the longitudinal muscular band as a site of selection for the deposit of the larvæ, their arrival in this situation being evidenced by a small linear hæmorrhage in the centre of the band. As the cyst forms, it is gradually extruded from the muscle and lies subperitoneally. In this position it is acted on by adhesions, and may be dragged away from the intestine leaving only a thin peritoneal strand indicating its point of origin. It is these loose cysts that finally rupture and cause septic peritonitis.

The adult worms are found attached to the mucous membrane of the

cæcum, but they may also extend down the large intestine for some distance.

The species of œsophagostomum has been kindly identified by Dr. LEIPER, who states it to be *Œsophagostomum apiostomum*.

The specimens, photographs and drawings which I show, fully illustrate this peculiar condition. The other specimens I am showing are not strictly tropical but they deal with blood parasites.

The common mole is full of interest to the parasitologist, and I show specimens of two parasites found in its blood. The first is an endocorpuscular parasite, first described by THOMSON, and now named *Elleipsisoma thomsoni* (Franca), the other is the trypanosome *(Trypanosoma talpæ)*. The reason I draw your attention to them is that I believe they are connected with each other, and that, probably, the trypanosome is developed from the endocorpuscular parasite. My investigation is, however, very incomplete, but the specimens and the drawings I show illustrate, what I take to be, intermediate forms.

Alongside these specimens are specimens of flagellates in the gut of mole fleas. It is possible that they are developmental stages in the flea of the mole trypanosome.

DEMONSTRATION BY MAJOR W. S. HARRISON, R.A.M.C.

(1) *A specimen of blood intensely infected with malignant tertian parasites.* Approximately 75 per cent. of the red cells were infected, many of them containing two, three, and occasionally four parasites. There were large numbers of young gametes. The case was from a beggar woman; she developed coma shortly after the specimens were taken, and a smear of the brain substance shows the usual intense infection of the blood in the capillaries of the brain.

(2) *Larvæ of Ankylostoma duodenale.* The patient was an officer invalided from India with anæmia in December last. No ova were found in the fæces in India. He had well-marked anæmia of the chlorotic type with 4,300,000 red corpuscles per c.m.m. and 38 per cent. hæmoglobin. There were 12,343 W.B.C. the leucocytosis being polymorphonuclear in character and there was no eosinophilia. He was treated with thymol in December and again in February by which time his hæmoglobin had risen to 60 per cent.; ankylostoma ova could only be found with difficulty on this occasion but a hatched specimen produced numerous larvæ. On March 12th his hæmoglobin had risen to 85 per cent. and there was now a very marked eosinophilia, the blood census being now polymorphonuclears 27 per cent., lymphocytes 23·4 per cent., large mononuclears 12·4 per cent., eosinophiles 36 per cent., and mast cells 1 per cent. Ova was still present in the fæces and it was interesting that although a large number of the worms had been expelled the eggs were found much more easily than on any former occasion.

(3) *A specimen of sputum from a case which presented physical signs of consolidation at the right apex, with severe dry cough and fever.* Tubercle of the lung was suspected but the stained specimens showed large quantities of threads of conidia of *Endomyces albicans.* These in places showed chromatin staining and the oval bodies were thought to be protozoal by the medical man in charge. The case came from Singapore, and the fever, etc., appeared to have been of short duration.

(4) *Specimens of pus from a case of Epizootic lymphangitis and smears from the spleen of a case of Histoplasmosis hominis* were shown together, to show the general resemblance of the two parasites.

(5) *A specimen of brain from a case of rabies* was also shewn, it contained negris bodies in great numbers.

SOME REMARKS ON KALA-AZAR IN THE SUDAN.

BY

L. BOUSFIELD, M.A., M.D. (CANTAB.), CAPT. R.A.M.C.

This disease, as met with in the Sudan, presents some rather striking differences to the description of the disease in text-books of tropical medicine.

A student on referring to such a text-book would, I think, form an opinion that the disease is only chronic and characterised by wasting, protuberance of the abdomen, great enlargement of the spleen, enlargement of the liver, and having alternating periods of pyrexia and apyrexia.

To mention some well-known authorities:—MANSON defines it as "an infective disease characterised by chronicity," and later says, "this condition of chronic fever, enlargement of the spleen and liver, emaciation and anæmia, may continue for months or even one or two years."

CASTELLANI and CHALMERS define it as "a subacute or chronic disease," and mention the same alternating periods of pyrexia and apyrexia, and state that finally the patient's appearance "is thin and wasted, with the abdomen much swollen and protuberant, the chest so thin that the ribs show clearly, the arms and legs wasted, the cheeks sunken, the nose sharp and the ankles puffy." "The total duration varies about seven months to two years."

ROGERS, in his excellent description of the disease, refers to it under the heading of "Fevers of Long Duration," and states that the fever lasts from a few months to several years. Later he remarks, "It literally kills by inches after most prolonged sufferings," and calls attention to the great wasting and the prominent tumid abdomen.

The descriptions in all these text-books apply very aptly to the subacute and chronic cases in the Sudan, but not to those suffering from an acute infection.

The writer has seen a case ending fatally in twenty-six days from the onset of symptoms.

Very careful inquiries were made about this case, and there appeared no reason to doubt that the patient was feeling, and appeared to others to

be, in perfect health twenty-seven days before her death from kala-azar, and, further, both she and her husband were most definite in their statements that she had had no illness whatever for three to four years previously; this was the most rapid case encountered. Out of twenty-three cases, positively diagnosed by finding the parasite, 21·7 per cent. died within thirteen weeks from the onset of symptoms.

THOMSON and MARSHALL in their report give five cases out of nineteen as terminating in two months (*i.e.*, 26 per cent.), and about 31·5 per cent. in four months or under, making a total of 57·5 per cent. ending fatally in four months or under.

These figures are worked out from the table in their report. The exact definition of a subacute or chronic disease I do not know, but the above figures show that this disease in the Sudan appears in many cases to run a rapidly fatal course.

There is always the difficulty of getting a correct history from natives, but now there have been so many giving the same history of short illness that there is no reasonable doubt about accepting it.

Possibly the reason for so many rapidly fatal cases being found in the Sudan is that splenic puncture has been undertaken frequently in acute fever cases, which showed none of the classical symptoms of the disease, as usually described.

Thus cases of kala-azar appear in the Sudan to fall naturally into three classes and might be classified under the following headings :—

1. *Acute*, i.e., those terminating within three months. These do not present the classical signs of prominent abdomen, greatly enlarged spleen and enlarged liver.

2. *Sub-acute*, i.e., terminating within six months;

3. *Chronic*, i.e., lasting six months or longer.

The two latter present the classical signs and appearance except that often wasting is not marked in the sub-acute cases.

Some of the main clinical features, etc., of these acute cases are :—

1. Intermittent fever, the temperature often rising to 102°-104°. From their histories these patients seem to have had no periods of apyrexia, but continuous fever from the onset.

2. The spleen is not enlarged to any great degree, extending either just to, or an inch or so beyond, the costal margin.

3. Absence of a protuberant abdomen—the appearance was often rather the reverse.

4. Liver very slightly, if at all, enlarged.

5. Very marked prostration and weakness, and rapid wasting.

6. Diarrhœa with blood-stained mucus was noted on several occasions.

7. The typical blood changes usually do not occur, and though there is no leucocytosis there is no marked leucopænia, and this appears also to hold good for most of the chronic cases in the Sudan.

Rogers states that 42 per cent. have less than 1,000 leucocytes per c.mm. and 72 per cent. less than 2,000.

In the acute cases the leucocytes usually number between 3,500 and 6,000, and even in the sub-acute and chronic cases the number is usually between 2,000 and 5,000, seldom falling below 3,000. The large mononuclear leucocytes vary enormously in number, having been noted between 8 per cent. and 44 per cent., usually between 20 per cent. and 30 per cent.

Personally, I am of opinion, though this is based on a very small experience, that leucopænia and a large mononuclear increase is not of very great value for the diagnosis of kala-azar in the Sudan, especially in the acute cases, but also in a lesser degree in the sub-acute and chronic, for in these the count is often 4,000-5,000, and the mononuclear increase means but little in a malarial country, especially when one remembers that Christophers and Stevens give 31 per cent. and Bastianella notes 41 per cent. as the average in malaria.

For diagnosis the examination of peripheral blood has produced very poor results in my hands, and only on two occasions have I found parasites in the peripheral blood, and both of these were acute cases.

Donovan, however, reports finding parasites in the peripheral blood in 93 per cent. of cases, and Marshall in the Sudan reports 86 per cent. positive results.

The examination of peripheral blood ought, therefore, undoubtedly to be done before proceeding to liver or spleen puncture, but it is doubtful if this is a very practical method for a hard worked, single handed doctor in the tropics, since Marshall states the parasites are very few, seldom averaging one per slide and the examination of three slides is usually necessary for diagnosis and in some cases eight films had to be examined

before reaching a positive result; this entails much laborious work and a large amount of spare time for microscopic work.

Further, one has to consider how often this method has failed in the hands of many competent workers.

Undoubtedly the easiest and surest method of finding the parasites is by means of splenic puncture, and probably the risks of this procedure have been greatly exaggerated, for a large series have now been performed by many workers without any bad results; for, as LEISHMAN notes, JEMMA and DI CRISTINA have punctured 200, NICOLLE and his fellow workers make no mention of any accidents and the writer has performed over 120 without any mishap.

The essentials for splenic puncture are :—

1. Warning the patient not to take a breath during the operation.
2. The use of a fine hypodermic needle.
3. Rapidity of action.
4. Holding the syringe loosely in the hand to prevent absolute fixation of the needle, should a breath be taken by the patient.
5. The usual aseptic precautions.

So far, in the Sudan, the disease appears to be mainly sporadic, and there is only slight evidence of an epidemic type, and that in a limited degree.

THOMSON and MARSHALL believe that the disease has been present in the Sudan for a long time, but the writer thinks this view may not be correct, basing his opinion on these three points: firstly, the very large number of acute cases; secondly, chronic cases of more than a year's duration are seldom found, while in India and Assam chronic sporadic cases appear to have been left in the wake of epidemics; and, thirdly, the absence of any history of any such epidemics amongst the natives in the past.

However, in favour of the view held by THOMSON and MARSHALL, Major LYLE CUMMINS informs me he feels sure he had two cases under his care in Kassala, in 1899, but did not recognise them as kala-azar.

Captain PATTON has now reported that he has been able to trace the parasite from the pre-flagellate stage, through the flagellate into the post-flagellate stage in both *Cimex rotundatus* and *Cimex lectularius*.

With reference to the Sudan I believe *C. rotundatus* has never yet

been identified, except in the newly added province, the Lado Enclave, whilst *C. lectularius* is met with in large numbers.

While *lectularius* is apparently omnipresent one is struck by the fact that kala-azar appears restricted to towns and villages on or adjacent to the rivers.

ROGERS notes that distance and paucity of population are barriers against the spread of the disease, and the former certainly holds good in the Sudan, but with reference to the population in the Kassala Province, Gedaref and its surrounding villages are far more densely populated than Mafaza, Gallabat, Tomat and Sofi, which are all affected by kala-azar.

Quite a considerable number of cases have occurred at Gallabat and Mafaza, while as far as is known none have contracted the disease at Gedaref, though intercommunication between these places is considerable.

Thus it seems probable that *C. lectularius* will not be found to transmit the disease in the Sudan.

In a small epidemic at Mafaza, burning down the huts proved very successful in stopping the epidemic, but against this one also has to note that most cases are single and do not appear to have passed on the disease to others living in the same huts, even when this precaution has not been adopted.

MARSHALL has succeeded in infecting monkeys *(Cercopithecus sabæus)*, and one young monkey kept in a cage with an infected monkey contracted the disease and died 34 days before the artificially infected monkey; he is following up these investigations.

The parasite has not yet been definitely found in dogs in the Sudan.

Two dogs were examined by me, and in one, an apparently healthy animal, which came from the hut of a very acute case, a few structures resembling Leishman parasites were found and depicted, but many did not possess a typical kineto-nucleus and it is doubtful if these were true Leishman parasites. The Kala-azar Commission in the Sudan inoculated five dogs with parasites, but were unable to recover any at the post-mortem examinations; the days of death after inoculation being 7th, 14th, 19th, 22nd and 52nd. All were inoculated from infected monkeys, except the one that survived to the 52nd day and which was inoculated from a spleenic puncture of a kala-azar patient.

As MARSHALL points out, this mortality is very striking and requires some explanation, which, at present, he is unable to give.

In *Leishmania infantum*, BASILE has found that fleas *(Pulex serraticeps* and *P. irritans)* can transmit the disease from dog to dog and from infected house to dog, so that this may be the means of transmission from monkey to monkey in the Sudan.

But, again, an apparent difficulty arises, for, as far as I am aware, the ordinary *Pulex irritans* is practically never found in any of the northern parts of the Sudan, and it seems improbable that natives would be infected from fleas on monkeys.

MARSHALL has succeeded in cultivating the parasite in 10 per cent. of citrate, and on Novy and McNeal's medium and Nicolle's modification.

He states the cultivation is easy, and with regard to the Novy and McNeal medium, the parasite appears to differ from the Indian variety, though LEISHMAN reports he has successfully cultivated the Indian parasite on this medium on one occasion.

Morphologically, the Sudan parasite is considered by all authorities to be indistinguishable from the Leishman parasite.

With reference to the treatment of this disease, up to the present, in the Sudan, I think I am right in saying that every form has failed.

Senega, suggested by Major ENSOR, promised well at first, but it seems probable that the improvements noted were only coincidents, for the disease is so well known to pass through more or less quiescent periods; however, it should be further tried as THOMSON and MARSHALL speak well of it.

Dr. ANDREW BALFOUR has tried soamin, without any good results, and he was kind enough to supply me with atoxyl, and this I employed with corrosive sublimate and fuchsin, each in turn in rotation, but without any beneficial results.

The large doses of quinine, recommended by ROGERS, have been tried by several, including the writer, without any permanently good results.

Dr. ROW's report on treatment of oriental sore by a vaccine made of a flagellate growth of *Leishmania tropica*, on Nicolle—Novy—McNeal medium, and sterilised by glycerine, perhaps opens a path of better treatment, and may, applied to kala-azar, lead to good results.

BALFOUR and ARCHIBALD have treated a case with "606" injections, and they say that they consider, from their observations, that a further trial of the drug should be undertaken.